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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,228	02/28/2006	Paul Stoffels	TIP-0058-USPCT	7472

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EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
09/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/570,228	**Applicant(s)** STOFFELS, PAUL	
	Examiner SAVITHA RAO	**Art Unit** 1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08/10/2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: ____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1, 6, 19-21 and 24-29*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614

/SAVITHA RAO/
Examiner, Art Unit 1614

Does NOT place the application in condition for allowance because: Applicants arguments in response dated 08/10/2009 in respone to the final rejection has been considered but are deemed partially unpersuasivr.
Applicant's arguments with reference to the 112 rejection is found to be persuasive and the 112 rejection set forth on pages 2-3 of the rejection is therefore withdrawn. Examiner would like to acknowledge other arguments presented by the applicant in their response specifically with respect to the 103 rejection which the examiner finds unpersuasive:
Applicants argue the the cited references do not disclose or suggest the combination as instantly claimed: Applicant is reminded again that it is the combination of the refemeces which renders the instant claims obvious. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).
In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Guillemont teaches both isoforms of TMC278 and suggest combination of that with Tenofovir or lamivudine for use as a medicine for HIV 1 treatment. Emtricitabine is a functional equivalent of lamivudine as taught by Hazen et al. who teaches that emtricitabine is a nucleoside reverse transcriptase inhibitor similar to lamivudine with antiviral activity against HIV-1 which share a common pathway through 2'-deoxycytidine kinase for conversion to their active nucleoside triphosphates. Clercq and Peiperl's teachings further provide motivation to an ordinarily skilled artisan to combine the three different categories (NNRTI, NtRTI and NRTI) of anti HIV drugs to treat HIV infections. All the references provide one of ordinary skill in the art motivation to combine a non-nucleoside reverse transcriptase inhibitor (NNRTI) with a Nucleotide reverse transcriptase inhibitor (NtRTI) and a nucleoside reverse transcriptase inhibitor (NRTI) and the advantages of using them in combination. All of the materials instantly claimed were known in the art to be useful to obtain an efficient anti HIV-1 drug. Accordingly, the references above provide motivation to one of ordinary skill in the art to formulate a medicine comprising the combination of the compounds taught by Guillemont which includes the two isomeric forms of TMC278 tenofovir, and emtricitabine for HIV 1 treatment. It is noted that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." Id. at 1742. Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients from within a prior art disclosure, to arrive at compositions "yielding no more than one would expect from such an arrangement". In this instance each ingredient disclosed is in a list as being substantially equivalent for the same purpose, i.e., either as a type of cancer to be treated or an anti-cancer drug amenable for use in treatment of said cancer types, thus, the very listing of each, despite the length of the list, provides clear motivation to choose any one or more from said list with the reasonable expectation of performing the disclosed function.
Moreover, NNRTIs, NtRTIs and NTRTI are individually known in the art as agents for treating HIV-1 conditions as shown supra, whose efficacy when administered alone is well established. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. In re Kerkhoven, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. In re Crockett, 126 U.S.P.Q. 186, 188 (CCPA 1960). The natural presumption that three individually known anti-HIV agents would, when combined, provide a third composition also useful for treating HIV flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (e.g. unexpected results) to rebut this natural presumption. Further, it is clear from the prior art that NNRTI combination with other drugs such as NtRTIs or NRTI's provide several advantages such as synergistic effect , reduction in the dosage and reduction of side effects. One skilled in the art would have been imbued with at least a reasonable expectation that a combination of NNRTI with NtRTI and NRTII would provide a composition with enhanced and beneficial effects.